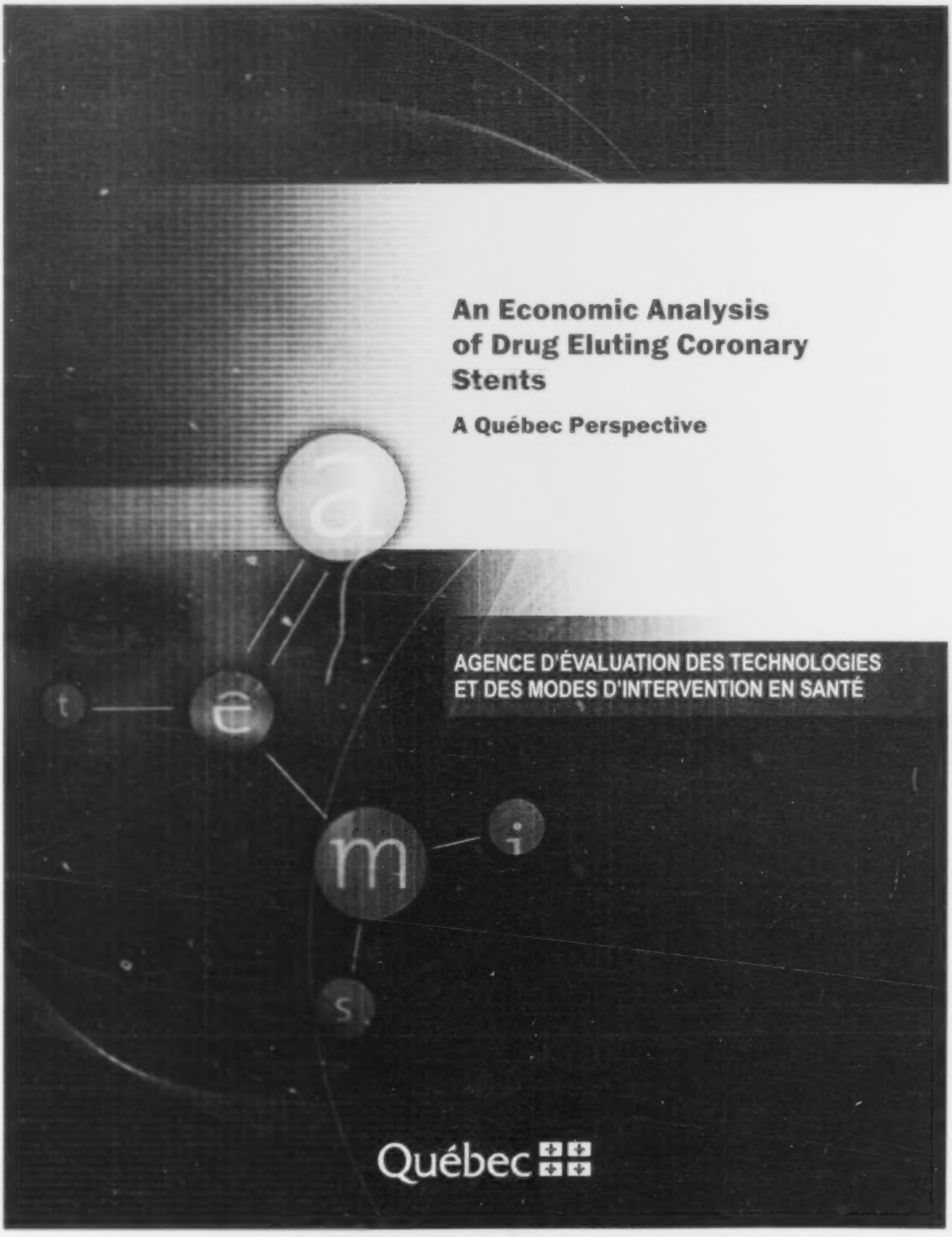
# An Economic Analysis of Drug Eluting Coronary Stents

## A Québec Perspective



# An Economic Analysis of Drug Eluting Coronary Stents

## A Québec Perspective

Report prepared for AETMIS
by James Brophy and Lonny Erickson

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*Agence d'évaluation des technologies et des modes d'intervention en santé*
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# MISSION

The mission of the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) is to contribute to improving the Québec health-care system and to participate in the implementation of the Québec government's scientific policy. To accomplish this, the Agency advises and supports the Minister of Health and Social Services as well as the decision-makers in the health care system, in matters concerning the assessment of health services and technologies. The Agency makes recommendations based on scientific reports assessing the introduction, diffusion and use of health technologies, including technical aids for disabled persons, as well as the modes of providing and organizing services. The assessments take into account many factors, such as efficacy, safety and efficiency, as well as ethical, social, organizational and economic implications.


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# FOREWORD

## ECONOMIC EVALUATION OF DRUG ELUTING CORONARY STENTS: A QUÉBEC PERSPECTIVE

Heart disease, and particularly coronary artery disease, has a considerable burden of mortality and morbidity in Québec and elsewhere. The problem is often blockage (stenosis) of coronary arteries which can be treated by reduction of risk factors, various medications and revascularization. Restoration of coronary circulation was originally achieved by coronary bypass surgery, however in recent years less invasive techniques such as balloon angioplasty have been developed. This technique involves insertion of a small balloon via a catheter into the artery followed by expansion to open the blocked vessel and placement of metal stents to prevent restenosis. Stents are endoprostheses made of a fine cylindrical mesh of stainless steel placed inside coronary arteries to keep the affected sections of these vessels (dilated by balloon angioplasty) open. These stents are now used in most interventions of this type in Québec, however a certain number of patients may still develop restenosis requiring additional interventions.

A recent technological advance is the development of pharmaco-active stents which reduce risk of restenosis; however they do not reduce the risk of death or myocardial infarction compared to bare metal stents. These drug-eluting stents are being increasingly promoted but some controversy exists as to how many patients should receive these more effective, yet more expensive devices.

In this context, the Québec Ministry of Health and Social Services requested that the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) in collaboration with the *Réseau québécois de cardiologie tertiaire* (RQCT) undertake an assessment of drug-eluting stents. The present report deals with the economic aspects of introducing this device in the health-care system.

The analysis indicates that universal adoption of drug-eluting stents would significantly reduce rates of repeat revascularization interventions in Québec. However, under current epidemiological conditions and purchase costs it would represent a considerable budgetary investment for moderate benefits in terms of avoided revascularization interventions. Because of the relatively low rates of restenosis currently observed in Québec, a much more cost-effective strategy currently would support limited use of drug-eluting stents given to carefully selected high-risk patients across the province, with the remainder of patients continuing to receive bare metal stents.

Systematic data collection on outcomes of patients treated with bare metal and drug-eluting stents is required to guide decision-making in coming years regarding optimal use of this new technology. This is a very rapidly developing area with an almost continuous influx of new information, therefore this issue should be re-examined in 6 to 12 months.

In submitting this report, AETMIS aims to contribute to optimal utilization of various resources in cardiology for the benefit of all affected patients.

**Luc Deschênes**
President and Chief Executive Officer

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This report was prepared at the request of the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) by **James Brophy**, M.D., PhD, and **Lonny Erickson**, MSc (PhD candidate).

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## CONFLICT OF INTEREST

None declared.

# EXECUTIVE SUMMARY

## CONTEXT AND OBJECTIVES

Most percutaneous coronary interventions (PCI) are now performed with the use of coronary stents. These stents are endoprostheses made of a fine cylindrical mesh of stainless steel placed inside coronary arteries to keep the affected sections of these vessels (dilated by balloon angioplasty) open. This technology has led to improvements in the safety of the procedure and to improved outcomes with a decreased incidence of restenosis requiring a repeat revascularization. Despite these improvements, restenosis leading to recurrent symptoms and the need for repeat procedures has remained a vexing problem.

Recent technological advances have led to the development of coronary stents coated with pharmacoactive agents which reduce restenosis. Studies of these drug eluting stents (DES) have been shown to decrease neointimal proliferation thereby further reducing angiographic restenosis rates and the subsequent need for repeat revascularization procedures. The evidence for the efficacy and safety of this technology in the short to medium term is excellent. However, this new technology is associated with substantial acquisition costs. At the time of writing of this report, a formal cost-effectiveness analysis has not yet been performed.

The present report attempts to quantify the benefits and costs associated with DES technology in order that informed resource allocation decisions may be made. The economic analysis was conducted from the perspective ot the Québec Ministry of Health and Social Services. This report has employed a systematic approach using evidence from both randomized clinical trials and from all-inclusive Québec medico-administrative databases describing local current practice patterns. The fact that objective data have been used to construct a realistic, transparent economic model and to provide Québec data-based estimates (and expected variability ranges for the model parameters) is a major strength of this report.

## EFFICACY OF DRUG ELUTING STENTS

A systematic review of all randomized trials comparing either sirolimus or paclitaxel, the two commercially available products, to bare metal stents has revealed no differences for mortality (Odds Ratio [OR] 1.03, 95% confidence interval [CI]: 0.56-1.92) or myocardial infarction (OR 0.93, 95% CI: 0.63-1.32). Drug eluting stents have been associated with a substantial decrease in the need for repeat target vessel revascularization (OR 0.26, 95% CI: 0.11-0.52). Current repeat revascularization rates in Québec following the use of bare metal stents have been determined from examination of medico-administrative databases (Med-Écho and RAMQ) from 1995 to 2000. During this period, the pooled average rate of a first reintervention in the 9 months following an initial PCI was 12.8% (95% CI: 10.4-16.0). Most of these reinterventions were PCI (82%), with the remainder being coronary artery bypass grafts (CABG; 18%).

## POTENTIAL IMPACT ON HEALTH CARE BUDGET

Based on the current purchase cost of $2,600 for DES, a baseline 9-month restenosis rate of 12.8%, and 14,000 angioplasties performed annually in Québec with an average of 1.7 stents per procedure, 100% substitution of bare metal stents with DES would require an additional $44.9 million of provincial funding. This would be associated with savings of $9.7 million, due to 1 527 fewer repeat revascularizations (of which 82% are PCI and 18% are CABG), leading to a net incremental cost of $35.2 million. Since no lives would be saved nor myocardial infarctions avoided, this benefit would cost $23,067 for each avoided repeat revascularization. Despite the fact that

no reduction in CABG rates was observed in the documented randomized trials, this benefit was included in the economic analysis to reflect the best available clinical data from Québec at the time of writing of this report.

## SELECTION OF HIGH-RISK PATIENTS TO RECEIVE DES

This analysis indicates, using the best currently available data, that universal use of DES would require significant additional health care funding even after savings are considered. Therefore, another potential scenario is to offer DES to a limited proportion of patients. In this situation, an optimal rate of DES use and selection criteria for the most deserving patients must be determined. If DES are only available for a limited number of patients, clinicians will naturally try to identify categories of patients at highest risk for restenosis to maximize potential benefit. There are several patient and angiographic features that are associated with increased risk of repeat revascularization, including diabetes, lesion length and vessel diameter. It is currently unknown to what extent high-risk patients prone to repeat revascularization can be identified in Québec. However, observations from medico-administrative databases indicate that diabetics make up 20% of the patient population receiving PCI and have a relative risk (RR) of restenosis 1.53 times that of non-diabetics. Given the presence of other potential clinical features to identify high-risk patients, it seems plausible that experienced clinicians using a combination of clinical and angiographic predictors may be capable of identifying patients with increased RR of 2 to 3.

## POTENTIAL RATES OF PENETRATION OF DES

The goal of this report is not to define a specific ceiling for this technology but rather to expose in a transparent fashion the costs and benefits that different penetrations of this technology will produce. An approximate 20-40% level has recently been suggested by an expert panel of Québec cardiologists (associated with the *Réseau québécois de cardiologie tertiaire*) as being clinically appropriate. Given that the baseline 9-month restenosis rate is currently 12.8% with bare metal stents in Québec, applying a policy of allowing for a 20% DES implantation rate to the most deserving patients would assure that most high-risk cases would have access to this technology. If a DES rate of only 10% were provided, costs would be lower; however, many clinically identifiable high-risk patients would not be able to receive DES. Conversely at levels of greater than 30% DES, clinicians would be treating an increasing number of lower risk patients.

## COST IMPACT OF TARGETED USE OF DES

Using the 9 month baseline restenosis rate of 12.8%, and a 20% DES penetration rate applied selectively to high risk patients (RR = 2.67), the net incremental cost after allowing for savings due to avoided revascularizations would be $4.7 million with 651 repeat revascularization interventions avoided at an average cost of $7,200 per avoided procedure. Of the avoided repeat revascularizations, 82% would be angioplasties and 18% would be coronary artery bypass surgeries. In this scenario, the breakeven cost, whereby the savings in reduced repeat revascularizations associated with DES completely offsets the additional purchase cost, occurs at a DES purchase price of $1,663. Corresponding breakeven costs would be $1,266 for 60% DES use (with selection of patients with a RR of 1.7 to receive DES) and $1,161 for 100% DES use. As the percentage of DES increases, incremental savings as a percentage of total expenditures fall and the cost per revascularization avoided increases.

## LIMITATIONS OF THE CURRENT ANALYSIS

Although this analysis is the most extensive analysis yet performed and tailored to the Québec environment, there are a number of limitations such as the absence of considera-

tion of the impact of additional funding for DES on other potential interventions competing for the same limited budget. Also, the potential for additional benefits of DES due to treatment expansion to include patients not presently eligible for a percutaneous intervention has not been considered. There is also some uncertainty regarding the actual rate of restenosis in Québec with BMS currently used. Also, if patients that otherwise might undergo CABG can be directed to angioplasty due to DES use, then substantial savings could be incurred. Should new evidence become available applicable to the clinical reality in Québec, this model can be easily updated.

## IMPLICATIONS

Finally, irrespective of the level of financing adopted for DES, ethical considerations underpinning the universality of our health care system dictate that equally deserving patients should have equal access to this technology. This implies that this technology, at whatever designated level, should be available at all centres performing PCI and that similar selection criteria should be broadly applied to assure equal accessibility according to clinical need and not geographic location. It is also abundantly clear that an evaluation of the local results with DES is necessary to aid future decision-making regarding this technology. Details regarding the implantation of all coated stents should be recorded in a registry to facilitate this evaluation. The *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) and the *Réseau québécois de cardiologie tertiaire* would appear to be ideal guarantors for this registry.

# ABBREVIATIONS

| | |
|---|---|
| AETMIS | *Agence d'évaluation des technologies et des modes d'intervention en santé* |
| BMS | Bare Metal Stent |
| CABG | Coronary Artery Bypass Graft |
| CEDIT | *Comité d'Évaluation et de Diffusion des Innovations Technologiques* |
| CCN | Cardiac Care Network (Ontario) |
| CI | Confidence Interval |
| CCOHTA | Canadian Coordinating Office of Health Technology Assessment |
| DES | Drug-Eluting Stent |
| HTA | Health Technology Assessment |
| ICD | International Classification of Diseases |
| INAHTA | International Network of Agencies for Health Technology Assessment |
| ISR | In-Stent Restenosis |
| MUHC | McGill University Health Centre |
| NICE | National Institute for Clinical Excellence |
| OR | Odds Ratio |
| PCI | Percutaneous Coronary Intervention |
| PTCA | Percutaneous Transluminal Coronary Angioplasty |
| QALY | Quality Adjusted Life-Years |
| RAMQ | *Régie de l'assurance maladie du Québec* |
| RQCT | *Réseau québécois de cardiologie tertiaire* |
| RR | Relative Risk |
| RSR | Restenosis Rates |
| RVH | Royal Victoria Hospital (McGill University Health Centre) |
| TAU | Technology Assessment Unit, McGill University Health Centre |

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# 1 INTRODUCTION

Percutaneous coronary interventions (PCIs) are an important group of non-surgical technologies that have been shown to improve the symptoms associated with coronary artery disease by percutaneous catheter manipulation. Initially this intervention was termed percutaneous transluminal coronary angioplasty (PTCA) and involved balloon angioplasty at the site of coronary artery narrowing. PCI now refers to the constellation of different techniques capable of relieving coronary narrowing or obstruction. In Québec, the majority of PCIs are now performed with the aid of intracoronary stents[1]. Other techniques including rotational atherectomy, directional atherectomy, extraction atherectomy, laser angioplasty, and brachytherapy are uncommonly used in the Québec context and will not be further addressed in this report.

Although PCI has not been shown to decrease death or myocardial infarction rates when compared to other treatment modalities [Bucher et al., 2000], it does provide important quality of life improvements over medical therapy and at lower risk and costs than mechanical revascularization by coronary bypass surgery. These positive health benefits coupled with technological advances resulting in improved safety profiles have led to an expanding number of PCIs worldwide, including Québec. For example, the complication of sudden arterial occlusion leading to acute myocardial infarction and urgent bypass surgery has been largely eliminated by the use of coronary stenting. Immediate angiographic and procedural success rates with PCI are now very high.

The major remaining problem associated with PCI is restenosis, which generally occurs within 6-9 months of the procedure and is principally due to neointimal hyperplasia. The magnitude of this problem has also been reduced, but not eliminated, by the use of coronary stenting. Notwithstanding that a recent meta-analysis of bare metal stents (BMS) suggested that their incremental value decreases sharply once a utilization rate of 50% is attained [Brophy et al., 2003], current practice now incorporates stents in approximately 90% of angioplasties. Recent studies with a new generation of drug eluting stents (DES), often released in a controlled manner from biocompatible polymer coating (an antimitotic agent) that act as a drug reservoir, have been shown to decrease neointimal proliferation thereby further decreasing angiographic restenosis rates and the subsequent need for repeat revascularization procedures in the short to medium term.

Beyond uncertainties regarding their long term results and safety, an important and as yet largely unstudied issue centers on the cost-effectiveness of this new technology. As resources for health care are scarce, it is important to perform an economic evaluation in order to explicitly evaluate this new technology. Therefore this report compares the use of drug eluting stents to uncoated stents under a variety of different scenarios in an attempt to provide insights regarding the cost-effectiveness of this technology compared to bare metal stenting. The perspective adopted is that of the Québec Ministry of Health and Social Services

1 Coronary stents are endoprostheses made of a fine cylindrical mesh of stainless steel placed inside coronary arteries to keep the affected sections of these vessels (dilated by balloon angioplasty) open.

# 2 BACKGROUND INFORMATION AND DATA

A number of different systematic approaches, including literature searches and use of medico-administrative databases, have been employed to identify all pertinent background information or data necessary for this economic evaluation. The presentation of published data will distinguish between efficacy, cost-effectiveness, and evaluations done by health technology assessment agencies or other organizations. In the last part of this section, medico-administrative data related to revascularization procedures performed in Québec will be presented.

## 2.1 EFFICACY

### 2.1.1 Literature search strategy

The PubMed database was searched (December 16, 1998-December 16, 2003) using the keywords: drug* AND restenosis and resulted in 1,051 references. The titles of these papers were screened to identify randomized clinical trials comparing coronary stents eluting antimitotic agents with uncoated stents. The Internet was also searched using the above keywords, including 3 websites dedicated to disseminating results from recent cardiovascular trials[2]. Trials published only in abstract form were included. References from identified studies as well as references from recent review articles on drug eluting stents were also searched for relevant papers.

### 2.1.2 Search results

Before performing an economic analysis, the improved efficacy of drug eluting stents must be confirmed. It is well established that the best experimental design to determine efficacy comes from randomized clinical trials and that a meta-analysis of randomized trials gives the most unbiased estimate of the treatment effect accompanied by the greatest precision. A recent meta-analysis [Babapulle et al., 2004] identified 15 randomized trials [Stone et al., 2004; Colombo et al., 2003; Grube et al., 2003a; Grube et al., 2003b; Grube et al., 2003c; Moses et al., 2003; O'Neill et al., 2003; Park et al., 2003; Schampaert et al., 2003; Schofer et al., 2003; Heldman et al., 2002; Grube, 2002; Morice et al., 2002; Serruys et al., 2002; Gershlick et al., 2001] comparing drug eluting to uncoated stents including 11 involving sirolimus and paclitaxel, the two commercially available products. The pooled analysis of these 11 trials involving 5,090 patients revealed no differences for mortality (OR 1.03, 95% CI: 0.56-1.92) or myocardial infarction (OR 0.93, 95% CI: 0.63-1.32). The absolute restenosis rate (generally 6 to 9 months post-intervention) was reduced from 29.3% with uncoated stents to 8.9% with the drug eluting stents (OR 0.17, 95% CI: 0.06-0.40). A corresponding decrease in the need for repeat target vessel revascularization was also observed (OR 0.26, 95% CI: 0.11-0.52). Subsequent coronary artery bypass use was very small in both groups with no differences noted. The inclusion of the 4 trials examining other drug eluting stents did not substantially change these estimates.

Although there is an abundance of evidence regarding the treatment of de novo lesions, there is much less quality information on the use of drug eluting stents to treat in-stent restenosis and no randomized clinical trials. The first clinical experience with sirolimus-eluting stents for the treatment of in-stent restenosis (ISR) involved only 16 patients and at four-month follow-up, three patients (20%) had angiographic evidence of restenosis [Degertekin et al., 2003]. Although there was no control group, the authors concluded that sirolimus eluting stents in patients with severe in-stent restenosis lesions effectively limit neointimal formation and recurrent restenosis. Another observation study of 25 patients with in-stent restenosis receiving sirolimus coated stents showed only 1 patient (4%) developed restenosis at 1 year [Sousa et al., 2003]. In

2. Available: www.scimd.com, www.theheart.org, www.clinicaltrialresults.org

contrast, the RESEARCH registry [Peck, 2003] examined a sub-group of 57 patients treated with coated stents for in-stent restenosis and found no significant differences when compared with results from 66 age-matched controls that were treated at the centre during the prior six months with bare metal stents.

Estimates for the rate of restenosis when treating in-stent restenosis with bare metal stents may be estimated by examining the control arms from the randomized trials of brachytherapy trials. This would suggest that restenosis rates are in the vicinity of 55% with repeat procedures at approximately 45% [Bennett, 2003]. Due to trial design, this may be an overestimate, similar to the overestimate of primary restenosis rates seen in randomized trials due to compulsory protocol driven angiography. The effect of variability in the estimate of this parameter will be examined in sensitivity analyses.

In conclusion, this systematic review of the literature demonstrated no differences in clinical outcomes of death, myocardial infarction or coronary artery bypass surgery between bare stents and drug eluting stents for the treatment of de novo lesions. However, there was an important decrease in restenosis rates and the need for repeat PCI. There is less data to evaluate the role of drug eluting stents for in-stent restenosis but indirect comparisons suggest that a reduction in restenosis and the need for repeat revascularization may also be expected in this population.

## 2.2 COST-EFFECTIVENESS

### 2.2.1 Literature search strategy

A similar systematic search of the medical electronic literature (PubMed, MEDLINE) was performed using the key words drug eluting stents (198 references), cost-effectiveness (37,170 reference) and the combination (7 references). In addition, the health technology assessment (HTA) databases managed by the International Network of Agencies for Health Technology Assessment (INAHTA) in collaboration with its UK member Centre for Reviews and Dissemination at York University (6 references) were searched. Although there are few formal peer reviewed published cost-effectiveness studies, there are no shortage of opinions and non-peer review publications. Using the Google Web search engine a total of 3,250 hits were found using the key words "cost-effectiveness of drug eluting stents".

### 2.2.2 Search results

The electronic database search for economic studies of drug eluting stents in the peer review literature found 4 references [Faxon, 2004; Kereiakes, 2003; Lemos et al., 2003; O'Neill and Leon, 2003]. However, these were not true economic evaluations (but rather editorial opinions on the future role of this technology) and consequently were not retained for further discussion. Using the Google search engine, one formal economic study by Harvard investigators was identified that was published in a peer reviewed journal not presently indexed by PubMed [Greenberg et al., 2003][3]. These investigators, who have received grants from the device industry, suggest that drug-eluting stents may be cost-effective for most patients undergoing PCI in the United States.

In a report published in May 2004, these conclusions were restated by the Drug-Eluting Stent Task Force (formed by the Society for Cardiovascular Angiography and Interventions in the United States); however this group mentions that minimal variations in the hypotheses in this analysis can modify the results and the conclusions of the economic analysis [Hodgson et al., 2004].

3. A recent article by these authors was published and indexed in PubMed [Greenberg et al., 2004], which contains the same analysis and data as in the article from 2003. In addition, two co-authors, Cohen and Bakhai, are the principal authors of a cost-effectiveness study published in August 2004. This study, associated with the SIRIUS clinical trial, has basically the same conclusions.

TABLE 1

**Comparisons of assumptions in the American published cost-effectiveness model with actual Québec data**

| CHARACTERISTIC | US DATA* | QUÉBEC DATA |
|---|---|---|
| Mean restenosis rate | 14.0% (between 1 and 12 months) | 12.8% (at 9 months) |
| Cost of restenosis | $25,000[a,b] | $4,507[b] |
| Cost difference between DES and BMS (average number of stents per patient) | $3,684[b] (1.4)[c] | $3,230[b] (1.7)[d] |
| Relative risk reduction with DES | 0.80[e] | 0.74[f] |

* Source: Greenberg et al., 2003

a According to Medicare data
b Costs are given in Canadian dollars
c Based on clinical trials of BMS
d According to a group of experts from the RQCT
e Based on one DES efficacy study
f Based on systematic review of efficacy from all randomized trials investigating DES efficacy [Babapulle et al., 2004]

There may be a number of concerns about direct application of results of the study by Greenberg et al. to the Québec environment, given the assumptions used in their calculations (see Table 1). The large differences between the parameter estimates used in their model and Québec data renders their model and conclusions unsuitable for the Québec context. These authors question the cost-effectiveness of routine use of drug eluting stents in patients with a low expected clinical restenosis rate (<10%).

## 2.3 HEALTH TECHNOLOGY ASSESSMENTS

### 2.3.1 Literature search strategy

The search of the INAHTA's databases helped also to identify assessment reports issued by national or regional HTA agencies on drug eluting stents. This consultation was completed by a manual search of the specific HTA agencies of Canada, United States, France, England, Spain, Sweden and Australia, and other Canadian organizations.

### 2.3.2 Search results

Consultation of the Web sites of national health technology assessment agencies revealed that only United Kingdom, France, Australia and Spain (Catalan) had produced reports on this technology. The National Institute for Clinical Excellence (NICE) in the United Kingdom issued a guidance for coated stents in October 2003. This organization concluded that drug eluting stents were a significant medical advance and should "be recommended in PCI for patients with symptomatic coronary artery disease (CAD), in whom the target artery is less than 3 mm in caliber (internal diameter) or the lesion is longer than 15 mm. This guidance for the use of DES does not apply to people who have had an MI in the preceding 24 hours, or for whom there is angiographic evidence of thrombus in the target artery" [NICE, 2003].

However in the UK, angioplasty is much more restricted than in Québec and the budgetary impact of the drug eluting stents was predicted to be relatively modest in their environment.

The 2002 Australian report [MSAC, 2002] concluded that although there was a potential for decreased costs due to a reduction in the need for repeat PCIs, there was insufficient evidence to allow for a formal assessment of cost-effectiveness. At that time, they assessed this technology as essentially experimental and as such, should be the subject of continuing research including a system for ongoing monitoring and evaluation established to assess long term efficacy and safety. A more up-to-date report is on-going as few would still share the opinion that this technology is experimental.

In France, the *Comité d'Évaluation et de Diffusion des Innovations Technologiques* (CEDIT) issued a statement in October 2002 recognizing the potential of drug eluting stents and recommending their use according to established indications determined by the medical literature [CEDIT, 2002]. However it was also recognized that further data collection through registries and cost-effectiveness analyses should be performed in the future.

In 2003, the Catalan Agency for Health Technology Assessment and Research published an assessment of drug eluting stents [Oliva and Espallargues, 2003]. This systematic review of the efficacy, effectiveness and safety of drug eluting stents for the treatment of coronary restenosis also examined its cost, and impact on the health of the population and the organization of the health system in Spain. These authors concluded that there is good-quality scientific evidence from randomized clinical trials that suggests that the sirolimus stent is efficacious and safe in the prevention of angiographic restenosis and that this might be a cost-effective intervention. These authors suggest that drug eluting stents might become cost neutral at a price of 1,939 euros ($3,180 CDN). However, the pertinence of these results may be questioned as their economic model assumed that uncoated stents cost 1,150 euros ($1,886 CDN) and that 20% of patients treated with a conventional stent would require a repeat revascularization. As will be demonstrated, both these assumptions seem far from the Québec reality, in which uncoated stents cost only $700 CDN, and near 13% of patients require repeat revascularization (see details in Section 2.4.1).

On a provincial level, the Cardiac Care Network (CCN) of Ontario has submitted recommendations to the Ontario Ministry of Health and Long-Term Care suggesting that a budget for 40% coverage with drug eluting stents is appropriate for 2003 and that it should increase to 60% in 2004 [CCN, 2003]. This report has been widely quoted by Québec cardiologists as supporting evidence for similar utilization rates here. However examination of this report shows it to be uniquely comprised of expert opinion with no systematic quantitative review of efficacy, safety or cost. The Ontario Ministry of Health has not accepted these recommendations but rather has provided a one time supplemental budget of $12 million which was expected to provide coated stents for 20% of angioplasty cases for the fiscal year 2003-4. The Medical Advisory Secretariat of the Ministry is currently conducting a field evaluation of DES in Ontario.

On a local level, in July 2003 the Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC) produced an evaluation of this technology based on best available evidence [Brophy, 2003]. This report concluded that based on an annual volume of 1,200 PCIs, at the RVH-MUHC hospital, a policy of replacing bare metal stents with the new coated versions might avoid the need for a repeat angioplasty for approximately 100 patients with a net cost in the vicinity of $2 million per year. Consequently a switch to DES was not endorsed in this report.

In summary, this review of different HTA agencies and other organizations confirms that the efficacy of this technology has been well accepted but that there remains a need for a thorough economic analysis, particularly within the local context, to assist decision makers as to the role the drug eluting stents should play and on the subsequent question of resource allocation. The Canadian Coordinating Office of Health Technology Assessment (CCOHTA) is conducting a comprehensive

study of this subject but their final report is not expected until the end of the summer of 2004. However a detailed economic analysis is required in the interim and is the rationale for this report.

## 2.4 USE OF PCI AND REPEAT REVASCULARIZATIONS IN QUÉBEC

### 2.4.1 Sources and methods

To assess recent trends in the utilization of PCI, Québec hospital medico-administrative databases were examined to identify all patients undergoing a PCI procedure between April 1, 1995 and December 31, 2000. The *Régie de l'assurance maladie du Québec* (RAMQ) database identified physician visits and procedures, and Med-Écho database captures all hospitalizations including up to 15 discharge diagnoses coded using the 9th revision of the International Classification of Diseases (ICD-9). All databases were linked through the use of a unique and anonymous identifier thereby creating a longitudinal history of each patient's clinical outcomes following PCI. The validity of the physician services dataset to identify revascularized patients was confirmed by cross-linking with the hospital admission/discharge dataset. We were unable to locate a corresponding hospital record for less than 1% of patients. The reliability of the hospital medico-administrative databases in recording the number of coronary revascularizations has been previously validated [CETS, 1996]. Moreover, the coding accuracy of primary and secondary discharge diagnoses in the Québec hospitalization database for elderly persons with cardiovascular disorders has also been demonstrated [Levy et al., 1999].

### 2.4.2 Current revascularization rates in Québec

While randomized clinical trials provide the most reliable information on the efficacy of the new drug eluting stents, an estimate of the current true rate of restenosis with bare metal stents is best obtained from the provincial medico-administrative databases. The 29% estimate of restenosis and consequent revascularizations from the clinical trials may be seriously biased due to trial design, which mandated angiography at 6 months regardless of the presence of clinical symptoms.

To obtain unbiased estimates of restenosis in Québec, we examined the RAMQ medico-administrative databases for the period 1995-2000 (Table 2).

TABLE 2

**Annual number of PCIs, and CABGs from 1995-2000**

| YEAR | TOTAL NUMBER PCIs | NUMBER WITH STENTS (% OF TOTAL PCIs) | NUMBER CABGs |
|---|---|---|---|
| **1995** | 6,585 | 520 (7.9%) | 5,474 |
| **1996** | 6,579 | 1,498 (22.8%) | 5,508 |
| **1997** | 7,701 | 3,732 (48.5%) | 5,835 |
| **1998** | 8,776 | 5,723 (65.2%) | 6,007 |
| **1999** | 9,580 | 7,090 (74%) | 5,838 |
| **2000** | 11,206 | 9,262 (83%) | 6,277 |

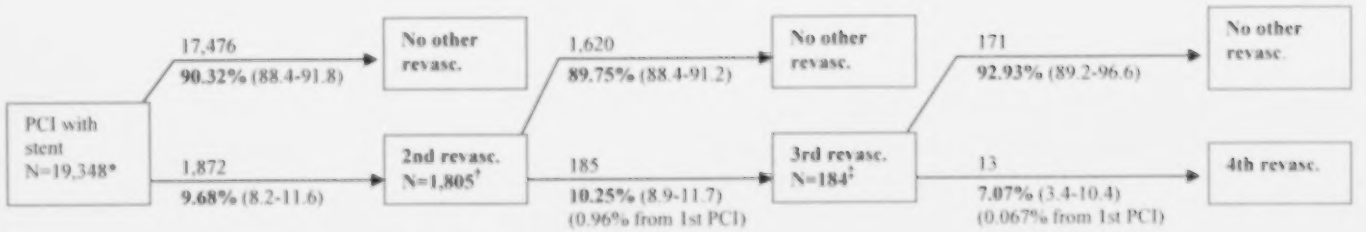
Sources: RAMQ, Med-Echo.
Note: To reflect increasing rates of these procedures in 2003, an estimate of 14,000 PCIs per year was used in the economic model.

In order to obtain data suggestive of "real" rates of restenosis measured by rates of revascularization procedures, we followed this combined multiyear cohort of 19,348 incident cases at 6 months and 16,746 cases at 9 months to assess their response to PCI and produce estimates for percentages of patients in each arm of the clinical pathway in Figure 3 (Chapter 3). Figures 1 and 2 show the flow of patients following an initial angioplasty with use of a bare metal stent allowing 6- and 9-month time windows for reinterventions. The individual yearly data that has been summarized in these figures is displayed in Appendices A to D.

During this period, the pooled rate of a first reintervention in the 6 months following PCI was 9.7% (95% CI: 8.2-11.6) much lower than that reported in the published trials. Also unlike the data in clinical trials, a substantial number of these first repeat revascularizations were coronary artery bypass surgeries. The pooled average of first repeat interventions in the 9 months following PCI was 12.8% (95% CI: 10.4-16.0). To gain some insight in the differential restenosis rates among higher risk patients, we also examined diabetic patients as a representative case study. The rate of re-interventions among diabetics was 13.0% (95% CI: 10.4-16.2) or odds ratio of 1.53 (95% CI: 1.37-1.71) compared to non-diabetics (see Appendix E). This suggests that patients with an increased risk may be relatively easily identified. The addition of other clinical and angiographic characteristics may be expected to further identify high risk patients. This possibility will be discussed in next chapter.

FIGURE 1

**Revascularizations in 6 months from Québec medico-administrative databases**




*Already excludes 629 deaths in hospital or before the 2nd revasc

† Excluding 43 deaths 24 obs. without hospit.

**Types of procedures (2nd revasc.):**
PCI=1579
84.35% (82.71-85.99)
CABG=293
15.65% (14.01-17.29)

‡ Excluding 1 obs. without hospit.

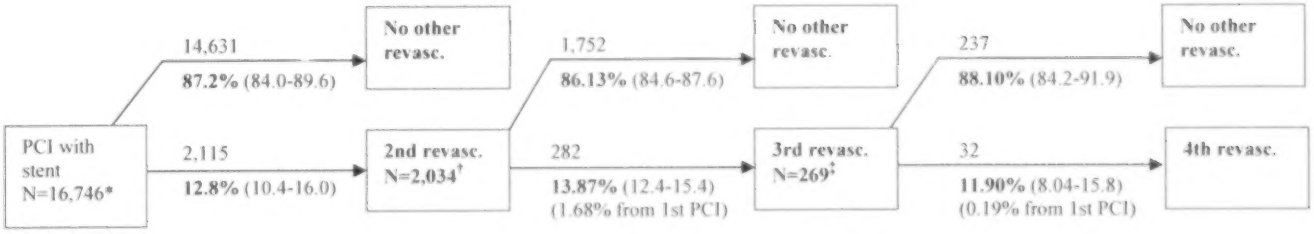
**Types of procedures (3rd revasc.):**
PCI=146
78.92% (73.02-84.82)
CABG=39
21.08% (15.18-26.98)

**Types of procedures (4th revasc.):**
PCI=10
76.92% (54.01-99.83)
CABG=3
23.08% (1.08-45.99)

Sources: RAMQ, Med-Echo

FIGURE 2

**Revascularizations in 9 months from Québec medico-administrative databases**




* Already excludes
611 deaths in hospital or
before the 2nd revasc

† Excluding
47 deaths
34 obs. without hospit.

‡ Excluding
6 deaths
7 obs. without hospit.

**Types of procedures (2nd revasc.)**
PCI=1,759
83.17% (81.58-84.76)
CABG=356
16.83% (15.24-18.42)

**Types of procedures (3rd revasc.)**
PCI=210
74.47% (69.37-79.57)
CABG=72
25.53% (20.43-30.63)

**Types of procedures (4th revasc.)**
PCI=22
68.75% (52.69-84.81)
CABG=10
31.25% (15.19-47.31)

Sources: RAMQ, Med-Écho

# 3 THE ECONOMIC MODEL

The principal characteristic of an economic analysis is "the comparative evaluation of alternative courses of action in terms of both their costs and consequences" [Drummond et al., 1997]. This report specifically compares the use of drug eluting stents (DES) to uncoated bare metal stents (BMS) under varying degrees of penetration and selection of patients at elevated risk of restenosis. Care has been taken to use a systematic approach to parameter estimation and all references and assumptions are explicit. Specifically, drug eluting stent efficacy has been determined from the overview results of the high quality randomized trials identified from the literature search described in Section 2.1.2.

This model is an extension and update of the economic model previously published in the McGill University Health Centre report on the use of drug eluting stents published by the Technology Assessment Unit in 2003 [Brophy, 2003] and now accurately reflects the practice profile in Québec as determined by an examination of medico-administrative databases from 1995-2000 (see section 2.4.2). The patients examined in this analysis are restricted to "incident" cases (defined as those with no previous angioplasties in the 6 or 9 months preceding the initial stent procedure). Following the initial intervention, a percentage of patients will require a repeat revascularization within 6 to 9 months due to restenosis of the initially treated vessel. Subsequently, a minority of patients may even require a third or exceptionally a fourth intervention for recurrent restenosis. The actual observed rate of revascularizations in the Québec population, freed from any constraint of the artificial world of clinical trials, is used in our economic model. Therefore although no reduction in the use of coronary artery bypass surgery with coated stents was seen in the clinical trials, our model allowed such reductions due to its use of actual clinical data for patients following an initial PCI from medico-administrative databases (Med-Écho and RAMQ) in the province of Québec.

The fact that systematic, objective data have been used to construct a realistic, transparent economic model and to provide local Québec data-based estimates and expected variability ranges for the model parameters is a major strength of this analysis.

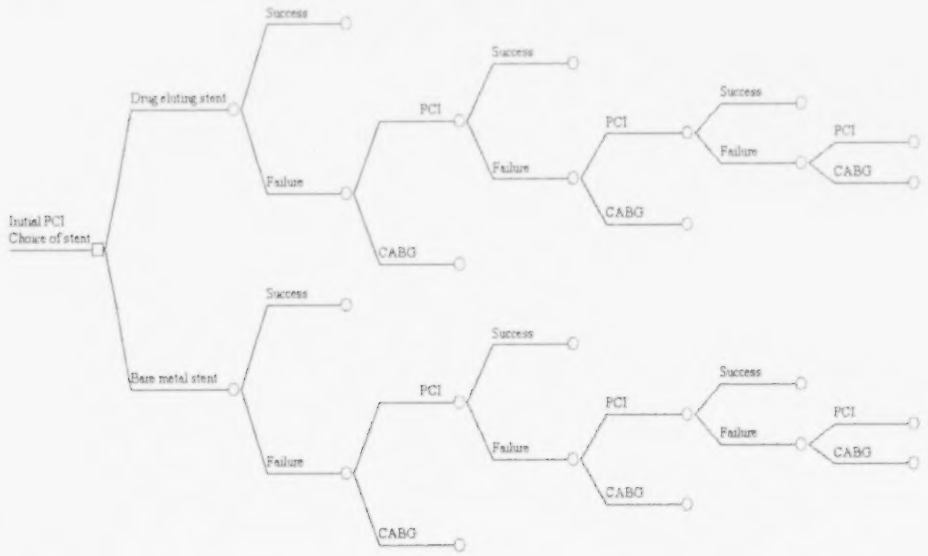
## 3.1 THE CLINICAL PATHWAY USED FOR ANALYSIS

Although there may be some concerns regarding long-term results of drug eluting stents, their established short to medium term efficacy in reducing repeat revascularizations has propelled the case for an economic analysis. The efficacy data for the model, based on the systematic review described in Section 2.1.2, showed no difference in the rate of procedural success or complications (deaths, myocardial infarction) between drug eluting and bare metal stents. The derived economic model therefore does not consider these outcomes and uses the clinical pathway illustrated in Figure 3.

This model allows up to 3 re-interventions following the initial PCI even though the medico-administrative data showed that less than 0.1% of the original cohort would require that many repeat procedures. The occurrence of coronary artery bypass surgery is considered a terminal endpoint.

FIGURE 3

**Clinical pathway for patients undergoing PCI with coronary stents in economic model**




Note: success is defined as the absence of a repeat revascularization procedure.

In the randomized trials, DES have resulted only in reductions in the need for repeat angioplasties and not in the need for bypass surgeries. However, data from the RAMQ and Med-Écho databases indicate that in current Québec practice, perhaps due to an unselected patient population, the early repeat intervention in a substantial number of cases is not an angioplasty but bypass surgery (Appendix D). Following the logic of allowing observed data to drive our economic model, a reduction in cardiac surgeries as a consequence of the expected overall reduction in repeat revascularizations associated with drug eluting stents was permitted in the model.

## 3.2 INPUT PARAMETERS

The economic model uses different input variables related to revascularization numbers and rates observed in Québec as well as the costs of these procedures. However, if it is assumed that only a limited number of the new drug eluting stents will be available for patients, the most important input parameter is the relative risk of restenosis rate of high-risk patients selected to receive DES. Some explanations are given about this variable after presenting values of input parameters used in the model, ranges of these values for sensitivity analysis and sources for these parameters (Table 3).

TABLE 3

**Values of input parameters in economic model, sources, and ranges of values used in sensitivity analyses**

| PARAMETER | VALUE IN BASE MODEL | RANGE FOR SENSITIVITY ANALYSIS | SOURCE(S) |
|---|---|---|---|
| Annual number of angioplasties in Québec | 14,000 | 14,000-15,000 | RAMQ<br>Med-Écho |
| Average cost of angioplasty, including $707 in medical professional fees (stent costs are excluded) | $4,507 | $4,000- $5,000 | RAMQ, MUHC-TAU report |
| Repeat revascularization rate, bare stents (following 1st intervention) | 12.8% | 9.7 -20% | RAMQ, Med-Écho 1995-2000 |
| Repeat revascularization risk reduction, drug eluting stents (following 1st intervention) | 0.74 | 0.48-0.89 | Meta-analysis of 11 randomized clinical trials* (95% CI) |
| Ratio of restenosis rates DES/BMS post PCI # 2 and post PCI #3 | 0.5 | 0.2-0.8 | Expert opinion |
| RR for restenosis of high-risk patients selected to receive DES | 2.67 | 1-6 | Large range based on theoretical model (Figure 4) |
| Repeat revascularization rate, bare stents (following 2nd intervention) | 13.9%<br>(1.08 times rate following 1st intervention) | 12-16% | RAMQ, Med-Écho 1995-2000 |
| Repeat revascularization rate, bare stents (following 3rd intervention) | 15.0%<br>(1.17 times rate following 1st intervention) | 10-20% | RAMQ, Med-Écho 1995-2000 |
| % of patients going to PCI vs. CABG | | | RAMQ, Med-Écho 1995-2000 |
| after 1st PCI | 83% | 78-88% | |
| 2nd PCI | 74% | 69-79% | |
| 3rd PCI | 69% | 64-74% | |
| Average number of stents per procedure (all interventions) | 1.7 | 1.2-2.2 | RQCT expert panel |
| Cost of uncoated stent | $700 | $600-$800 | MUHC-RVH |
| Cost of drug eluting stent (base model) | $2,600 | $2,000-$2,800 | MUHC-RVH |
| Cost of CABG (including $1,025 in medical professional fees) | $15,025 | $9,825-$17,025 | RAMQ,<br>MUHC-RVH median (and 25%-75% range) |

* Source: Babapulle et al., 2004.

### 3.2.1 Revascularization numbers and rates

Québec data have already been presented in the previous chapter; however, these data present a range of values which could be used in the economic model. While it is accepted that most cases of restenosis occur within 6 months, there may be some cases presenting later. Extending the window for restenosis to 9 months leads to higher reintervention rates (12.8%, 95% CI: 10.4-16.0), although these rates are possibly somewhat contaminated by the development of new stenoses other than the originally treated lesion. We utilize the 9 month restenosis rate of 12.8% in our base case, and 6 month restenosis rate (9.7%) as well as rates of 15% and 20% are included in the sensitivity analyses to examine the impact of this parameter on results and conclusions of this report. The overall estimate of the efficacy of drug eluting stents versus bare metal stents has been determined by a hierarchical pooling of all randomized clinical trials [Babapulle et al., 2004].

### 3.2.2 Selection of high-risk patients for DES

In the case where DES are only available for a limited number of patients, clinicians will naturally try to identify patients at highest risk for restenosis so as to maximize potential benefit. There are several patient and angiographic features that are associated with increased risk of repeat revascularization, including diabetes, lesion length and vessel diameter. The clinical success in identifying high-risk patients is unknown but Québec medico-administrative databases reveal that 20% of the population are diabetic and their repeat revascularization rate was approximately 1.5 times that of the non-diabetic population (13.0% vs. 8.9%). Therefore, at least for the scenario of 20% use of DES, we can consider that clinicians should on average be able to select an appropriate higher risk group of patients with a RR of at least 1.5.

By combining a constellation of other risk factors, it seems plausible that selection of high-risk patients with a baseline relative risk of restenosis 2-3 times that of remaining patients could be achieved by clinicians. However, we have no hard data on the actual ability of clinicians to accurately select patients at high risk of stenosis at a given percentage of DES. In the absence of this data, it is essential to examine more closely the theoretical implications of this type of selection of high-risk patients to receive DES.

First of all, the effect of *depletion of susceptibles* must be considered. The selection of high-risk patients implies a corresponding lowering of risk in the remaining group of patients. Because the overall combined patient population has not changed, the total combined risk of revascularization must remain constant. The following example illustrates this point: If 100 patients undergo the initial PCI and the baseline revascularization rate for BMS is 10%, we would expect a total of 10 cases of revascularization in the 100 patient cohort and 2 cases of revascularization in a randomly selected subgroup of 20 patients. The remaining group would be expected to have 8 cases of restenosis per 80 patients. The baseline risk of restenosis is 0.1 in the two groups (2/20 and 8/80 patients); the relative risk is therefore equal to 1. However, if it were possible to select 20 higher risk patients so that a total of 4 cases of restenosis occurred (instead of 2), the number of expected cases of restenosis in the remaining group of patients would decrease from 8 to 6. In this case the risk of restenosis would be $4/20=0.2$ in the high-risk group and $6/80=0.075$ in the remaining patients. This produces a risk ratio (RR) of $0.2/0.075=2.67$ between the two groups. If the total number of cases of restenosis selected reached six, the relative risk would therefore reach 6 ($6/20 \div 4/80$). In this scenario, a RR of 6 corresponds to the median level of selection of cases between RR=1 (no selection) and RR=$\infty$ (level of selection at which all cases of restenosis are selected). A RR of 2,67 corresponds to the lower quartile of this distribution. We can illustrate the unlikely theoretical case of perfect selection (where RR=$\infty$) by the ratio of restenosis with perfect selection versus random selection in a cohort of 100 patients

(Table 4 and Figure 4). This allows maximal theoretical values for each scenario to be established and also the determination of intermediate quartiles at various levels of selection between these maximal values and the baseline case in which there is no selection whatsoever (RR=1).

To consider the advantages of various different percentages of DES penetration, it is instructive to examine the maximum theoretical risk ratios which could ideally be obtained by clinicians. These ratios vary according to the percentage of patients offered DES, and the baseline restenosis rate. To determine these maximal values we can consider, for a group of 100 patients receiving an initial PCI, the ideal case in which the 10 patients who would develop restenosis in the cohort were in the group selected to receive DES. In concrete terms, this ideal scenario can be compared to the scenario in which there is random selection of patients for DES (RR=1), illustrated in Table 4.

This exercise clearly illustrates that due to the low 10% restenosis rate, the impact of patient selection is potentially very high at lower levels of DES penetration and rapidly becomes negligible as values increase over 50%. This relationship is illustrated in Figure 4. This figure indicates the theoretical maximum ratio of cases in the high-risk cohort compared to baseline if all patients at risk are captured in the DES cohort (upper line). Random use of DES (i.e. no patient selection) would imply this ratio being 1 for all scenarios. Intermediate scenarios can be added to produce the five following illustrative scenarios for selection of high-risk patients into the DES cohort:

- Random patient selection (RR=1);
- Lower quartile between 1 and median value;
- Median between 1 and max theoretical value;
- Upper quartile between median and theoretical maximum value;
- Maximum theoretical selection.

While this model does not decrease our uncertainty about the actual patient selection that can be attained in current clinical practice in Québec, this will allow impacts on assumptions regarding these important parameters to be made explicit. For the economic model, we used values corresponding to the lower quartile (between no selection and median selection of high-risk patients) as a reasonable value which could be attained in clinical practice. For example, at a 20% level of DES use, this implies a RR of 2.67 for those selected for DES versus the 80% not selected for DES.

Finally, it illustrates without a doubt that due to the fact the best available evidence indicates current revascularization rates in Québec are below 20%, there is little possible improvement in the economic parameters of using DES by selecting high-risk patients in scenarios where they are given to over 50% of patients. This is due to the effect of depletion of susceptible patients (and is clearly illustrated in Figures 8 and 9 (p. 20-21) by the convergence of lines for various scenarios). These parameters merit further exploration in the medium and long term, particularly with regards to what extent selection of high-risk patients can occur for various scenarios.

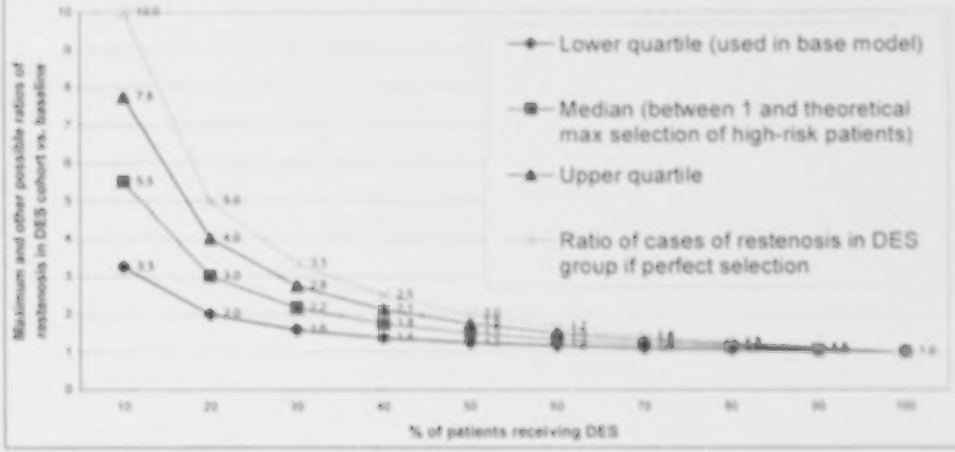
TABLE 4

**Maximum possible ratios of cases in DES cohorts with perfect selection (RR=∞) of high-risk patients (10% restenosis rate, reference group of 100 patients)**

| % DES | BASELINE NUMBER OF CASES WITH RESTENOSIS, RANDOM PATIENT SELECTION | MAXIMUM POSSIBLE NUMBER OF CASES | DIFFERENCE | RATIO OF CASES IN DES COHORT IN SCENARIO WITH PERFECT SELECTION VS. RANDOM DISTRIBUTION (RR=1) |
|---|---|---|---|---|
| 10 | 1 | 10 | 9 | 10 |
| 20 | 2 | 10 | 8 | 5 |
| 30 | 3 | 10 | 7 | 3.3 |
| 40 | 4 | 10 | 6 | 2.5 |
| 50 | 5 | 10 | 5 | 2.0 |
| 60 | 6 | 10 | 4 | 1.7 |
| 70 | 7 | 10 | 3 | 1.4 |
| 80 | 8 | 10 | 2 | 1.25 |
| 90 | 9 | 10 | 1 | 1.11 |
| 100 | 10 | 10 | 0 | 1 |

FIGURE 4

**Theoretical maximum and intermediate distributions of restenosis per % DES scenarios, reference group of 100 patients**


Maximum and other possible ratios of restenosis in DES cohort vs. baseline
% of patients receiving DES
Lower quartile (used in base model)
Median (between 1 and theoretical max selection of high-risk patients)
Upper quartile
Ratio of cases of restenosis in DES group if perfect selection

### 3.2.3 Cost estimates

The direct hospital costs of PCI and CABG (including nursing and other personnel as well as medical and surgical supplies for the intervention and medical fees) and likely distributions surrounding the uncertainty of these estimates were obtained from the MUHC-Royal Victoria Hospital Finance Department. The relative and absolute values of these costs are similar to the cost of cardiovascular procedures reported by others in the medical literature, particularly from Canadian sources [O'Brian et al., 2000; Cohen et al., 1999]. Coronary stent purchase costs are also those paid at the Royal Victoria Hospital (MUHC). Hospital costs did not include an additional percentage for administration costs (a figure of 30% is often employed); however the impact of omission of this figure is minor as demonstrated by univariate sensitivity analyses.

## 3.3 MEASURES OF OUTCOMES

### 3.3.1 Main outcome measure: Avoided revascularization intervention

The health benefits of medical interventions are most usefully recorded in a readily quantifiable manner such as lives saved. Increasingly the value not only of reduced mortality, but also reduced morbidity has been recognized and the standard metric for benefit in economic analyses has become quality adjusted life-years (QALY) where health is rated on a scale from 0 (death) to 1 (perfect health). These standardized measures of benefit allow an easy comparison of the value of different therapies. However, the QALY measure has several drawbacks in the present analysis, as the benefits of drug eluting stents versus bare metal stents involve the avoidance of interventions (and associated short-term disutility), rather than avoiding death or permanent disability. We have therefore elected to measure health benefits in this economic analysis primarily by use of the surrogate endpoint of number of revascularization procedures avoided (PCI or CABG), indicating the estimated percentage of CABG for each scenario.

### 3.3.2 Derived outcome measures

Since information on costs are available, two different outcome measures can be derived from the benefit of avoided repeat revascularizations:

- Incremental cost of a drug eluting stent program: this measure is estimated by the total additional costs related to the purchase and use of DES minus the savings from avoided repeat revascularization interventions;
- Cost per avoided revascularization intervention: obtained by dividing the incremental cost of the program by the total number of revascularization procedures avoided.

### 3.3.3 Potential outcome measure: Cost per QALY gained

While a full study of the impact on revascularization interventions on quality of life in Québec is beyond the scope of this study, some basic estimates can be performed using recently published (but limited) data [Yock et al., 2003], which enable estimation of disutility values for angina, CABG, balloon angioplasty and stenting. Using the incremental cost estimate for the scenario with 20 % DES implementation and the number of avoided CABG and PCI, an estimate of cost per QALY gained for this scenario can be calculated. Due to the exploratory nature of this calculation, the result will be introduced in Chapter 5 (Discussion).

## 3.4 DISCOUNTING

Since there is a paucity of medium or long term data, the economic model examines only a 6 to 12 month window as the number of assumptions required to make a longer projection were too numerous and unstable to

provide any reliable information. Due to this narrow time frame, discounting of results has not been applied. The perspective is that of the Québec Ministry of Health and Social Services.

## 3.5 SENSITIVITY ANALYSIS

The cost-effectiveness analysis was constructed using Microsoft Excel spreadsheets (Microsoft Corporation, 2000). Univariate and multivariate sensitivity analyses were conducted using Monte Carlo simulations, performed using Crystal Ball computer software (Decisioneering Corporation, 2000).

# 4 RESULTS

## 4.1 COSTS AND BENEFITS OF POTENTIAL DES PROGRAMS

### 4.1.1 Limited use scenario: 20% DES implementation, 12.8% restenosis rate

Based on a cost of drug eluting stents at the current price of $2,600 and assuming use of an average of 1.7 stents per procedure, the complete introduction of DES would require an additional $44.9 million in the annual Québec health care budget. However, this would be associated with savings of $9.7 million, due to 1,527 fewer repeat revascularization interventions (18% CABG, 82% PCI), leading to a net incremental cost of $35.2 million. At a level of 20% DES penetration (allowing for selection of high-risk patients, RR=2.67), the net incremental cost after allowing for savings due to avoided revascularizations would be $4.7 million. In this scenario, 651 repeat revascularization interventions would be avoided at an average cost of $7,200 per avoided procedure (18% of which would be CABG, and 82% PCI).

### 4.1.2 Variation of % DES implementation and restenosis rates

*Impact on incremental cost of program*

Figure 5 presents the incremental cost of DES use under varying percentages of DES penetration, with restenosis rates of 9.7% (observed 6-month rate in Québec), 12.8% (observed 9-month rate in Québec), 15% and 20% (hypothetical rates). Higher restenosis rates do indeed reduce the total incremental cost of DES use. For example, for the scenario of 100% DES implementation, the net incremental cost for Québec would be $5 million lower ($30 million instead of $35 million) if the restenosis rate were 20% instead of the 12.8% rate which was used in the base model.

*Impact on cost per avoided revascularization intervention*

Figure 6 illustrates the impact on the cost per avoided revascularization intervention for varying scenarios of DES implementation. Using the 12.8% restenosis rates in the base model, we see that this cost increases from approx. $7,000 at 20% DES implementation to approx. $23,000 at 100% DES implementation. This same increase in cost per avoided revascularization intervention occurs at higher levels of restenosis (15% and 20%). For example if restenosis rates were 20% in Québec, the cost per avoided revascularization intervention of approx. $3,000 for 20% DES implementation would increase to approx. $13,000 at 100% DES use. These results indicate that this cost-effectiveness parameter is much more favourable at lower levels of DES implementation, regardless of whether the restenosis rate is 9.7% or 20%.

*Impact of % DES implementation on gains from selection of high-risk patients*

Considerable gains in cost-effectiveness are attained from the selection of patients at an increased risk for restenosis. However, due to the depletion of high-risk patients these gains diminish as the percentage of DES implementation rises. This can be illustrated by comparing three scenarios of selection of high-risk patients (as previously presented in Section 3.2.2):

- No selection of high-risk patients (RR=1);
- Reasonable selection of high-risk patients used in base models (lower quartile between RR=1 and median value; i.e. RR=2.67 for 20% DES);
- Enhanced selection of high-risk patients (median quartile between RR=1 and theoretical maximum value; i.e. RR=6 for 20% DES).

FIGURE 5

Incremental cost of DES use per baseline restenosis rate (RSR) and % implementation, allowing for selection of high-risk patients (RR=2.67 for 20% DES, lower quartile for other scenarios)

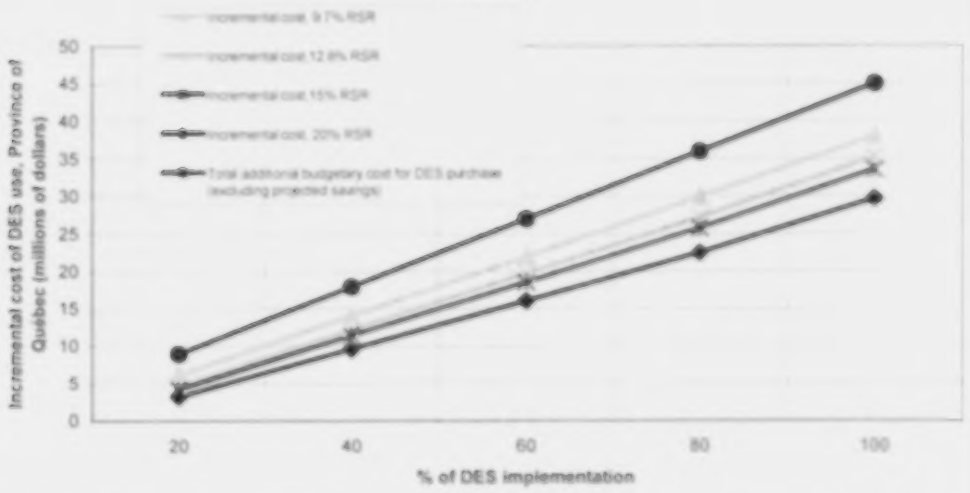



FIGURE 6

Cost per avoided revascularization intervention (approx. 18% CABG) vs % DES use and restenosis rate (allowing for selection of high-risk patients for DES, RR=2.67 for 20% DES, lower quartile for other % of DES)

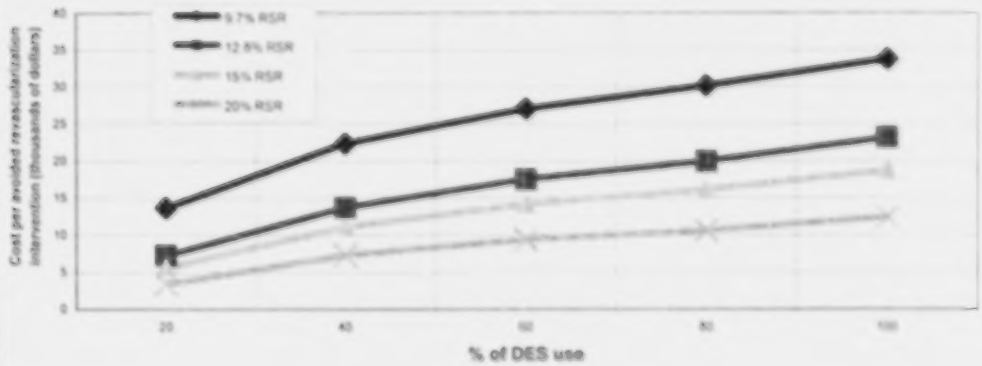


FIGURE 7

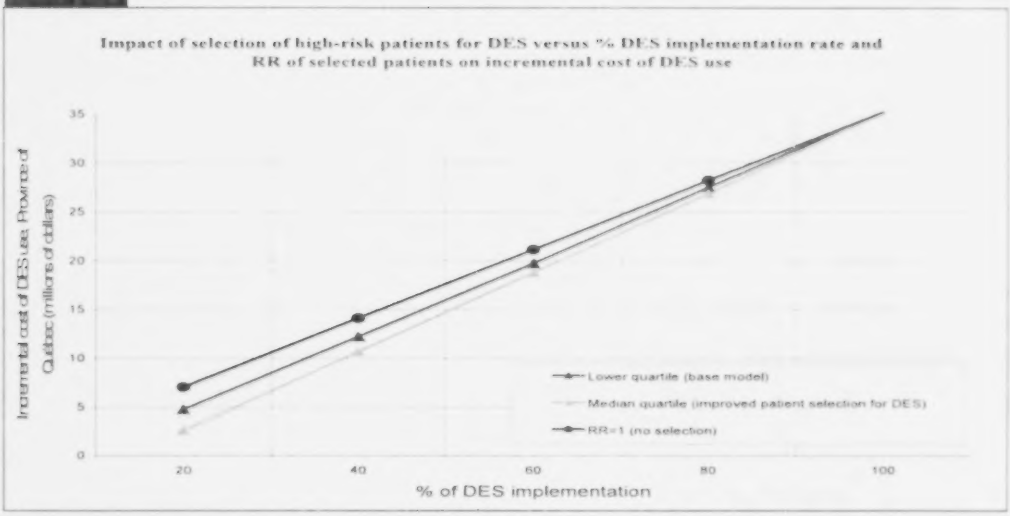



Figure 7 illustrates that the initial gain of $2.29 million dollars which could be obtained from reasonable patient selection (in reducing the incremental cost of DES) decreases to $1.9, $1.4, $0.7 million and $0 at 40%, 60%, 80% and 100% DES implementation respectively. These values are obtained from the difference in incremental cost between the line for RR=1 (no selection) and other scenarios of selection of high-risk patients for particular scenarios of DES implementation.

Figure 8 illustrates the impact of this same variation on the cost per avoided revascularization intervention, and shows that the impact of patient selection is even greater for this cost-effectiveness parameter. The result is that while costs per avoided revascularization intervention of near $10,000 can be attained with a reasonable level of selection of high-risk patients at DES implementation levels of 20-40%, even when an extremely high level of selection of high-risk patients is attained with DES implementation levels of 60-100%, the cost per avoided revascularization intervention is from $15,000 to $23,000. This is a classic example of diminishing returns from increased implementation of a more effective, yet more expensive health technology if a subgroup of high-risk patients can be selected for limited implementation of this technology.

### 4.1.3 Breakeven cost for DES

The hypothetical purchase cost of DES was calculated at which benefits of avoided treatment would offset the increased cost of DES implementation. These breakeven costs for DES under different scenarios of implementation rates are presented in Table 5. In the likely scenario of a 20% penetration applied to patients at medium to high risk of restenosis (RR = 2.67), the breakeven cost whereby savings associated with DES completely offset the additional purchase cost occurs at $1,663. For 100% DES implementation, the purchase cost must be over $500 lower, at $1,161.

FIGURE 8

**Impact of selection of high-risk patients for DES versus % DES implementation rate and RR of selected patients on cost per avoided revascularization intervention**

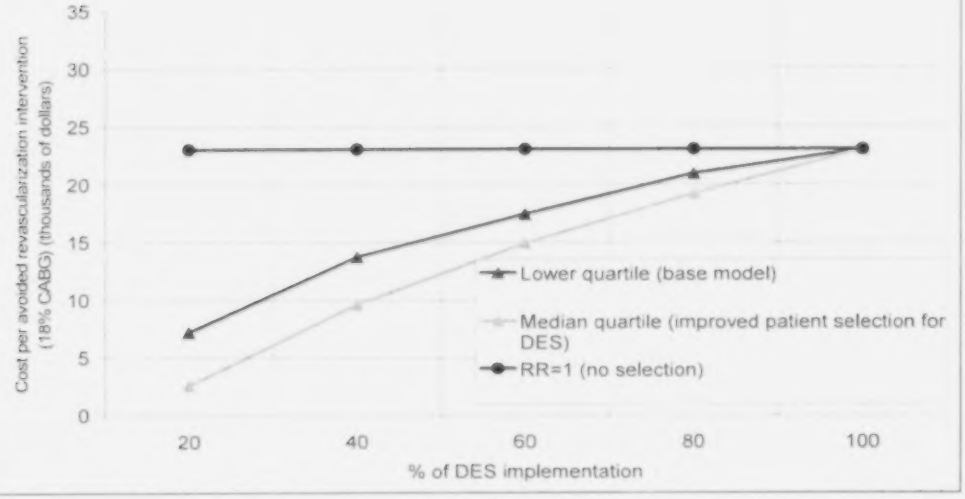



TABLE 5

**Breakeven costs for DES as a function of market penetration and ability to identify high-risk patients**

Breakeven unitary purchase cost of DES per scenario, % DES, 12.8% RSR

| % DES SCENARIO | RR=1, NO SELECTION | RR=LOWER QUARTILE | RR VALUE FOR PATIENTS RECEIVING DES |
|---|---|---|---|
| 20% DES | $1,161 | $1,663 | 2.67 |
| 60% DES | $1,161 | $1,266 | 1.7 |
| 100% DES | $1,161 | | 1 |

## 4.2 SENSITIVITY ANALYSES

### 4.2.1 Univariate sensitivity analyses

It must be appreciated that the parameters in this economic model are not exactly known and that their variability may influence the impact on incremental cost and the cost of avoided revascularizations. In the scenario with 20% DES implementation, we can examine that impact of varying the input parameters in the model to the extreme values presented in Table 3 (p. 12).

From our univariate sensitivity analyses (Appendices G and H), it is seen that the most important variables are the capacity to select high-risk patients for DES use, the cost of DES, the number of stents per procedure, the baseline revascularization rate with bare metal stents and the effectiveness of DES.

### 4.2.2 Multivariate Monte Carlo sensitivity analysis

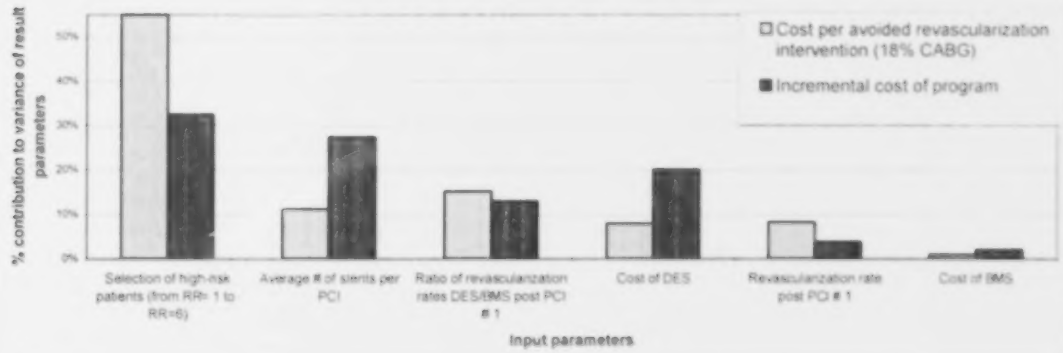
In order to examine cumulative potential effects of uncertainty in input parameters for this economic model, a probabilistic Monte Carlo analysis was performed using all parameters in the univariate sensitivity analyses, within the values indicated in Table 3 (p. 12). Triangular distributions from the base case value to extreme values were utilized with 1,000 trials per simulation. The results of the sensitivity analysis are presented in Figure 9. These results confirm the results of the univariate sensitivity analyses, and indicate that the five most important factors influencing cost per avoided revascularization intervention and the incremental cost of the program are the following:

- Ability to select high-risk patients (RR varied from 1 to 6);
- Average number of stents per PCI;
- Ratio of revascularization rates for DES/BMS;
- Cost of DES;
- Revascularization rate post PCI # 1;
- Cost of BMS.

No other parameters had an impact of over 1% in contribution to variance of the results. Therefore, in the short to medium term, if major variations occur in these parameters in Québec, an update of this economic model will be warranted to examine the impact on results, and resulting cost-effectiveness of potential scenarios for use of DES.

FIGURE 9

**Results of Monte Carlo sensitivity analysis: Impact on incremental cost of program & cost per avoided revascularization, 20% DES**



# 5 DISCUSSION

## 5.1 SPECIFIC CONTEXT OF QUÉBEC

Although there are numerous opinion pieces regarding the role of drug eluting stents, there are very few formal cost-effectiveness analyses. Several different national technology assessment groups have studied the clinical efficacy of DES but none have provided a detailed cost-effectiveness of this technology. One group of American investigators have published a cost-effectiveness study of this technology but their assumptions differ importantly from the Québec context. In the US, intervention costs and bare metal stent costs are much higher than in Canada, therefore the increased price of a DES is less significant relative to overall cost, increasing its cost-effectiveness. Also repeat revascularization rates in Québec are markedly different from those observed in this American study.

This report provides cost-effectiveness for drug eluting stents based on efficacy data from a systematic review of all the randomized trials comparing them to bare metal stents accompanied by an economic model based on contemporary observed Québec interventional cardiology practice patterns and using Québec costs. Regarding effectiveness, there is no proof that DES will alter mortality or myocardial infarction rates compared to bare metal stents. This prevents any calculation of cost-effectiveness ratios pertaining to lives saved or myocardial infarctions avoided.

## 5.2 QUALITY OF LIFE

However, use of DES will indeed reduce rates of angina and repeat revascularization interventions (PCI and CABG) and related short-term impacts on quality of life. A cost per QALY gained can be estimated using recently published values for disutility for these interventions [Yock et al., 2003] (detailed calculation in Appendix F). The cost per QALY gained is estimated at $96,523 in the base scenario with 20% of DES and a RR of selected patients of 2.67. Although the randomized trials have not shown any reduction in coronary artery bypass surgery our economic model does allow for this possibility, based on observed practice patterns following an initial percutaneous intervention.

If DES were to completely replace bare metal stents, purchase costs would rise by $44.9 million with $9.7 million in future savings from avoided revascularizations for a net incremental cost of $35.2 million. This would reduce repeat revascularizations by a projected 1,527 procedures annually at an average cost of approximately $23,000 per avoided procedure. Although various cost thresholds have been proposed in the literature [Laupacis et al., 1992], a value of $50,000 per life-year saved is often proposed in recent publications from the United States. However, Canadian society has not yet determined a threshold for willingness to pay to avoid a revascularization procedure. In the US, there has been some preliminary discussion on the willingness to pay to avoid a repeat procedure and an amount of approximately $10,000 US has been suggested [Greenberg et al., 2003].

## 5.3 SELECTION OF HIGH-RISK PATIENTS TO RECEIVE DES

If DES costs remain stable, the only way to reduce the cost per avoided repeat revascularization is to more successfully identify patients at increased risk (thus preventing more revascularizations per additional dollars spent to purchase DES). Medico-administrative data from the period 1995-2000 confirms clinical impressions that diabetics have an increased risk of repeat revascularizations (RR=1.53, 95% CI: 1.37-1.71). Other clinical and angiographic characteristics also predict the need for repeat revascularizations and it seems likely that patients with a RR=2.67 can be reliably identified.

Under this scenario of 20% DES utilization, the additional funding would be $8.9 million with an incremental cost of $7 million after considering future savings from decreased procedures if DES are given to randomly allocated patients. This incremental cost decreases to $4.7 million if high-risk patients (RR=2.67) are selected.

At this level of patient selection, the cost of avoiding a repeat revascularization procedure is $7,200. As clinicians improve in their ability to risk stratify patients, the incremental costs and the cost per avoided procedure fall. For example, if clinicians could select patients extremely well and attain a RR=6, then a 20% DES rate could attain a cost of $2,600 per avoided repeat revascularization procedure. However, as the percentage of DES increases, the incremental savings as a percentage of total expenditures falls and the cost per revascularization avoided increases. Lower rates of DES use with a better selection of the highest risk patients favourably improve the cost per avoided revascularization ratio.

## 5.4 LIMITATIONS OF CURRENT ANALYSIS

Although this analysis is the most extensive analysis yet performed and tailored to the Québec environment, there are a number of limitations that must be noted. The opportunity costs, in other words the lost opportunities to invest elsewhere in the health care system, due to increased costs with DES technology have not been considered. Moreover, society has yet to decide how much value to accord the avoidance of a repeat revascularization and so the interpretation of the cost-effectiveness metric $/ avoided revascularization is difficult.

Also the economic model employed does not account for the possibility of DES as a treatment expansion, in other words the provision of stenting to patients who currently are deprived of angioplasty due to prohibitively high risks of restenosis or to individuals for whom DES implantation might be a substitute for bypass surgery. In this case, some patients who might otherwise be referred for a higher cost CABG might become candidates for lower priced angioplasty with DES. As another example, patients who remain symptomatic with medical therapy but are not surgical candidates, and for whom standard PCI carries too high a risk of a restenotic complication might possibly experience substantial long-term quality of life benefits with DES.

Clinical trials have not and likely will not be able to address this issue of treatment expansion. Consequently, it is very hard to attach any concrete estimates of cost-effectiveness for expansion of utilization but the greatest health benefits and best cost-effectiveness indices are potentially available for this group. Although difficult to quantify, the clinical desire to have the necessary flexibility to address these rather special situations must be appreciated.

## 5.5 EQUITY AND ETHICAL CONSIDERATIONS

Finally, irrespective of the level of financing adopted for DES, ethical considerations underpinning the universality of our health care system mandate that equally deserving patients should have equal access to this technology. This implies that this technology should be available at all centres performing PCI and that similar selection criteria should be broadly applied to assure equal accessibility according to clinical need and not geographic location.

The main obstacle to adoption of DES, beyond the uncertainty regarding long term results, is the required increase in funding for cardiology and health care in Québec in the context of limited health care dollars which should be directed to interventions which prevent a maximum of mortality and morbidity per dollar spent. It must be emphasized that the use of DES prevents only repeat revascularization (which is a valid goal but distinctly less important than directly saving lives). Based on this economic analysis, the universal introduction of DES would greatly increase expenditures with relatively limited benefits.

# 6 CONCLUSION

Accepting that the universal introduction of DES seems untenable in the current context from an economic viewpoint, what would the optimal rate of utilization be in Québec? The identification of high-risk patients certainly improves the cost-effectiveness of this technology but the present report can't supply a definitive answer, as societal values will ultimately determine the DES allocation rate. At the present stent costs, there appears to be little cost-effectiveness justification for high rates of DES implementation, due to low baseline restenosis rates with BMS and diminishing returns with increased use of DES. A substantial fall in the efficacy or price of DES or our ability to identify high-risk patients could substantially alter this conclusion. Fortunately the transparent economic model used in this report can be rapidly updated according to future evolutions in DES. It is pertinent to mention that the previously mentioned Drug-Eluting Stent Task Force (United States) also recognizes the usefulness of cost-effectiveness analysis in the elaboration of guidelines regarding the use of DES for high-risk patients who can obtain the most benefit [Hodgson et al., 2004]. The conclusions and recommendations of this group are in agreement with those of the present report.

Irrespective of the level of DES implantation that is finally accorded, it is abundantly clear that an evaluation of the results attained with this technology is necessary to aid future decision-making. Details regarding the implantation of all coated stents should be recorded in a registry to facilitate this evaluation. The actual capacity of clinicians to select high-risk patients should be documented, as well as more current rates of restenosis, both for BMS and for DES. The *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) and the *Réseau québécois de cardiologie tertiaire* would appear to be ideal guarantors for this registry.

Parallels exist between the introduction of drug eluting stents and the advent of bare stent technology [Kong et al., 2004]. The clinical, administrative, economic and ethical challenges in cardiovascular medicine are similar to those following the advent of hemodialysis [Kjellstrand, 1996], or low-osmolar contrast media for use in radiology and cardiology [CETS, 1990; 1991], and present new problems, dilemmas, and controversies regarding optimal use of expensive new technologies [Coats, 2001; Mattke, 2000]. However, carefully constructed and unbiased economic models supported by and updated with data reflecting the current clinical reality in Québec will help clinicians, administrators and patients in Québec to successfully navigate between this clinical Scylla and administrative Charybdis [Kong et al., 2004].

It must be acknowledged that this is a very rapidly developing area with an almost continuous influx of new information. Accordingly any recommendation in this document must be re-evaluated periodically as new evidence becomes available. It is suggested that the issue be re-examined no later than in 6 to 12 months.

# APPENDIX A

**Rates of 1st repeat revascularization after a stent (1995 – 2000)**

| YEAR | 6 MONTHS | | | 9 MONTHS | | |
|---|---|---|---|---|---|---|
| | **All Patients*** n/N† (%) | **Non-diabetics** n/N† (%) | **Diabetics** n/N† (%) | **All Patients*** n/N† (%) | **Non-diabetics** n/N† (%) | **Diabetics** n/N† (%) |
| **1995** | 28 / 241 (11.62%) | 16 / 183 (8.7%) | 12 / 58 (20.69%) | 22 / 128 (17.19%) | 13 / 94 (13.83%) | 9 / 34 (26.47%) |
| **1996** | 109 / 1,132 (9.63%) | 86 / 918 (9.4%) | 23 / 214 (10.75%) | 140 / 1,082 (12.94%) | 108 / 882 (12.2%) | 32 / 200 (16%) |
| **1997** | 333 / 3,068 (10.75%) | 246 / 2,470 (9.96%) | 87 / 598 (14.55%) | 424 / 2,972 (14.27%) | 316 / 2,399 (13.17%) | 108 / 573 (18.8%) |
| **1998** | 477 / 4,919 (9.70%) | 350 / 3,897 (8.98%) | 127 / 1,022 (12.43%) | 600 / 4,796 (12.51%) | 436 / 3,812 (11.44%) | 164 / 984 (16.67%) |
| **1999** | 567 / 6,124 (9.26%) | 404 / 4,888 (8.27 %) | 163 / 1,256 (12.98 %) | 719 / 5,984 (12%) | 511 / 4,776 (10.7%) | 208 / 1,208 (17.2%) |
| **2000** | 358 / 3,864 (9.27%) | 255 / 3,012 (8.47%) | 103 / 852 (12.09%) | 210 / 1,784 (11.77%) | 150 / 1,409 (10.65%) | 60 / 375 (16%) |
| **Pooled Average‡** | 9.7% CI: 8.2-11.6 | 8.9% CI: 7.3-10.8 | 13.0% CI: 10.4-16.2 | 12.8% CI: 10.4-16.0 | 11.7% CI: 9.3-14.8 | 17.3% CI: 14.3-20.8 |

Sources: RAMQ, Med-Écho.

* These are only patients who had no previous revascularizations in the 6 or 9 months respectively preceding their revascularization (i.e. incident cases of PCI). Consequently only partial data from 1995 and 2000 were used.

† n=number of revascularizations/N=number of patients.

‡ Weighted pooled average, based on a random effects model that includes the variation within each year as well as the variation between years. When there is not a lot of between year variation this approaches the simple average.

# APPENDIX B

**Rates of 2nd repeat revascularization after a stent, and a 1st repeat revascularization (PCI or CABG) 1995 – 2000**

| YEAR | 6 MONTHS | | | 9 MONTHS | | |
|---|---|---|---|---|---|---|
| | **All Patients*** n/N† (%) | **Non-diabetics** n/N† (%) | **Diabetics** n/N† (%) | **All Patients*** n/N† (%) | **Non-diabetics** n/N† (%) | **Diabetics** n/N† (%) |
| **1995** | 4 / 241 (1.7%) | 2 / 183 (1.1%) | 2 / 58 (3.4%) | 6 / 128 (4.7%) | 3 / 94 (3.2%) | 3 / 34 (8.8%) |
| **1996** | 13 / 1,132 (1.1%) | 11 / 918 (1.2%) | 2 / 214 (0.9%) | 19 / 1,082 (1.8%) | 16 / 882 (1.8%) | 3 / 200 (1.5%) |
| **1997** | 40 / 3,068 (1.3%) | 30 / 2,470 (1.2%) | 10 / 598 (1.7%) | 65 / 2,972 (2.2%) | 49 / 2,399 (2%) | 16 / 573 (2.8%) |
| **1998** | 42 / 4,919 (0.9%) | 30 / 3,897 (0.8%) | 12 / 1,022 (1.2%) | 84 / 4,796 (1.8%) | 63 / 3,812 (1.7%) | 21 / 984 (7.4%) |
| **1999** | 46 / 6,124 (0.8%) | 32 / 4,888 (0.7%) | 14 / 1,256 (1.1%) | 78 / 5,984 (1.3%) | 56 / 4,776 (1.2%) | 22 / 1,208 (1.8%) |
| **2000** | 40 / 3,864 (1.0%) | 27 / 3,012 (0.9%) | 13 / 852 (1.5%) | 30 / 1,784 (1.7%) | 20 / 1,409 (1.4%) | 10 / 375 (2.7%) |

Sources: RAMQ, Med-Écho

* These are only patients who had no previous revascularizations in the 6 or 9 months respectively preceding their revascularization (i.e. incident cases of PCI). Consequently only partial data from 1995 and 2000 were used.
† n=number of revascularizations/N=number of patients.

# APPENDIX C

**Rates of 3rd repeat revascularization after a stent, and a 1st and a 2nd repeat revascularization (PCI or CABG) 1995 – 2000**

| YEAR | 6 MONTHS | | | 9 MONTHS | | |
|---|---|---|---|---|---|---|
| | **All Patients*** n/N† (‰) | **Non-diabetics** n/N† (‰) | **Diabetics** n/N† (‰) | **All Patients*** n/N† (‰) | **Non-diabetics** n/N† (‰) | **Diabetics** n/N† (‰) |
| **1995** | 0 | 0 | 0 | 0 | 0 | 0 |
| **1996** | 1 / 1,132 (0.09‰) | 1 / 918 (0.11‰) | 0 | 1 / 1,082 (0.09‰) | 1 / 882 (0.11‰) | 0 |
| **1997** | 5 / 3,068 (0.16‰) | 4 / 2,470 (0.16 ‰) | 1 / 598 (0.17‰) | 13 / 2,972 (0.43‰) | 12 / 2,399 (0.50‰) | 1 / 573 (0.17‰) |
| **1998** | 4 / 4,919 (0.08‰) | 1 / 3,897 (0.03‰) | 3 / 1,022 (0.29‰) | 6 / 4,796 (0.13‰) | 3 / 3,812 (0.08‰) | 3 / 984 (0.30‰) |
| **1999** | 1 / 6,124 (0.02‰) | 0 | 1 / 1,256 (0.08‰) | 9 / 5,984 (0.15‰) | 6 / 4,776 (0.13‰) | 3 / 1,208 (0.25‰) |
| **2000** | 2 / 3,864 (0.05‰) | 1 / 3,012 (0.03‰) | 1 / 852 (0.08 ‰) | 3 / 1,784 (0.17‰) | 1 / 1,409 (0.07‰) | 2 / 375 (0.53‰) |

Sources: RAMQ, Med-Echo

* These are only patients who had no previous revascularizations in the 6 or 9 months respectively preceding their revascularization (i.e. incident cases of PCI). Consequently data from 1995 and 2000 were only partially used.
† n=number of revascularizations/N=number of patients

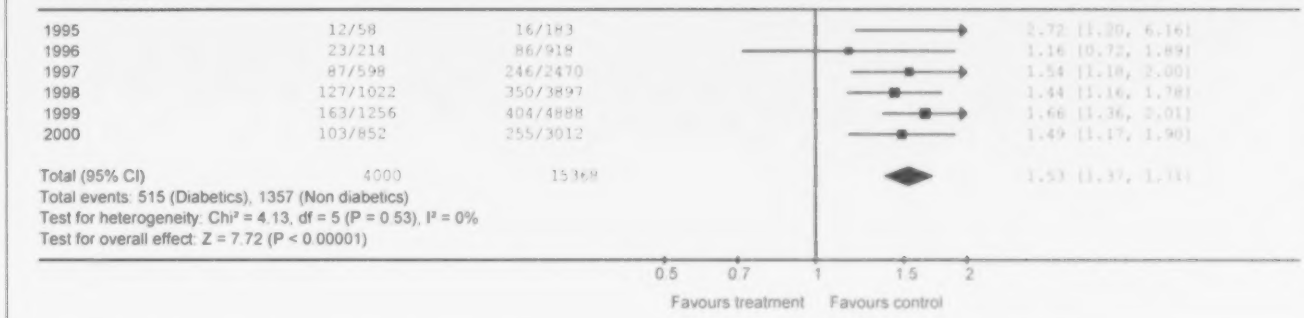
# APPENDIX D

**Distribution of 1st, 2nd, and 3rd repeat revascularization procedures**

| | 6 MONTHS | | | 9 MONTHS | | |
|---|---|---|---|---|---|---|
| | **1st repeat revasc.** | **2nd repeat revasc.** | **3rd repeat revasc.** | **1st repeat revasc.** | **2nd repeat revasc.** | **3rd repeat revasc.** |
| **PCI** | N=1,579 | N=146 | N=10 | N=1,759 | N=210 | N=22 |
| % | 84.35% | 78.92% | 76.92% | 83.17% | 74.47% | 68.75% |
| 95% CI | (82.71%-85.99%) | (73.02%-84.82%) | (54.01%-99.83%) | (81.58%-84.76%) | (69.37%-79.57%) | (52.69%-84.81%) |
| **CABG** | N=293 | N=39 | N=3 | N=356 | N=72 | N=10 |
| % | 15.65% | 21.08% | 23.08% | 16.83% | 25.53% | 31.25% |
| 95% CI | (14.01%-17.29%) | (15.18%-26.98) | (1.08%-45.99%) | (15.24%-18.42%) | (20.43%-30.63%) | (15.19%-47.31%) |
| **Total revasc.** | **1,872** | **185** | **13** | **2,115** | **282** | **32** |

## Odds ratio for repeat revascularizations for diabetics compared to non-diabetics*

Review: Revasc
Comparison: 01 Repeat revascularizations
Outcome: 01 Repeat revascularizations




* Based on data extracted from Québec medico-administrative databases (RAMQ – Med-Echo) from 1995-2000

# APPENDIX F

## SAMPLE CALCULATION FOR ESTIMATION OF COST PER QALY GAINED FOR DES USE

| EVENT | QALY VALUE |
|---|---|
| Return of anginal symptoms | -0.013 |
| Tradional balloon angioplasty | -0.04 |
| Primary stenting | -0.02 |
| CABG | -0.07 |

Source: Yock et al., 2003

Example: Implementation scenario: 20% DES, selection of high-risk patients for DES with RR=2.67.

Incremental cost = $4.7M, 651 avoided PCI (534 angioplasties, 117 CABG)

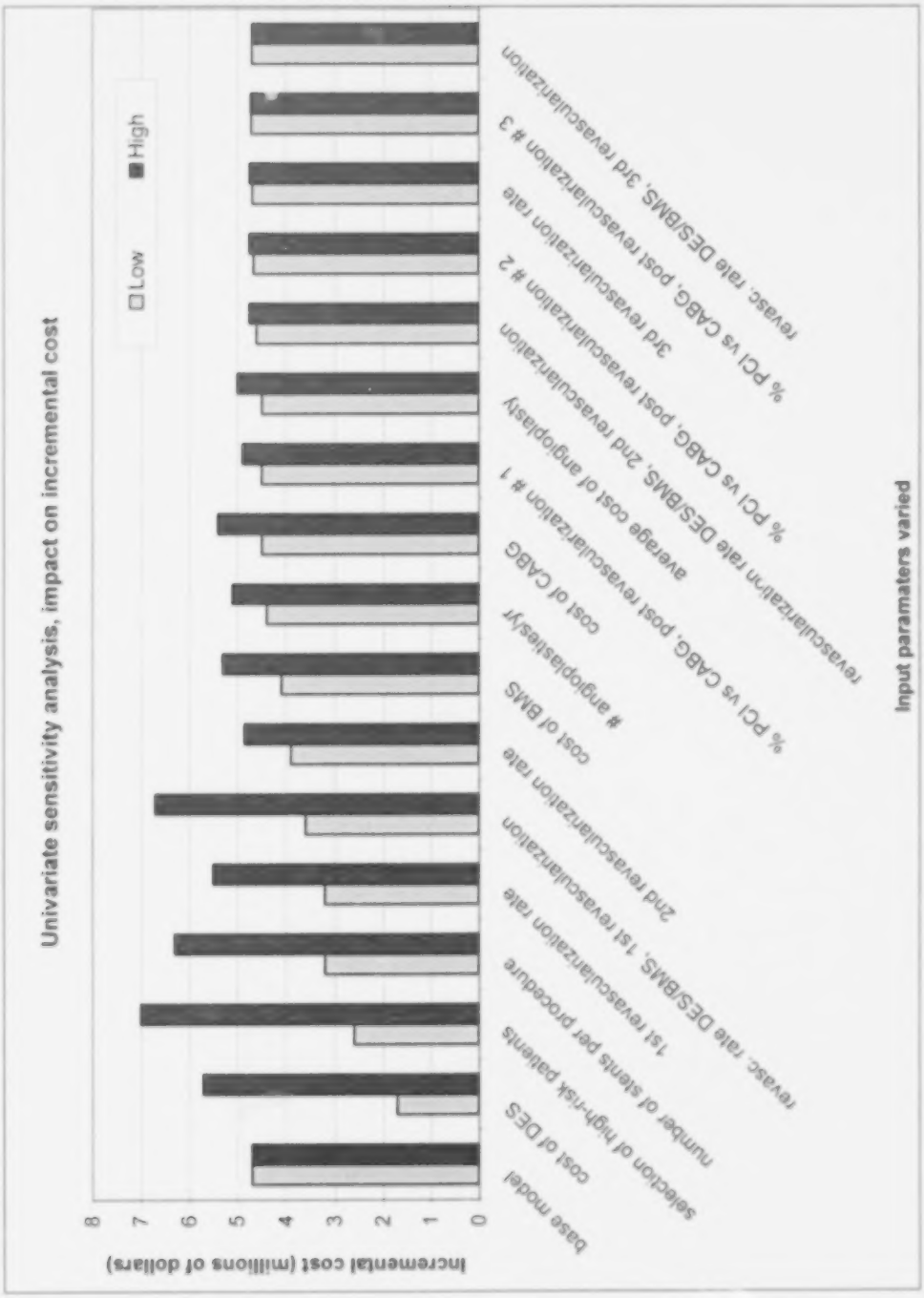
Assume that each reintervention is preceded by 4 weeks of anginal symptoms

Total QALY gain for $4.7M = gain from avoided PCIs + gain from avoided CABG

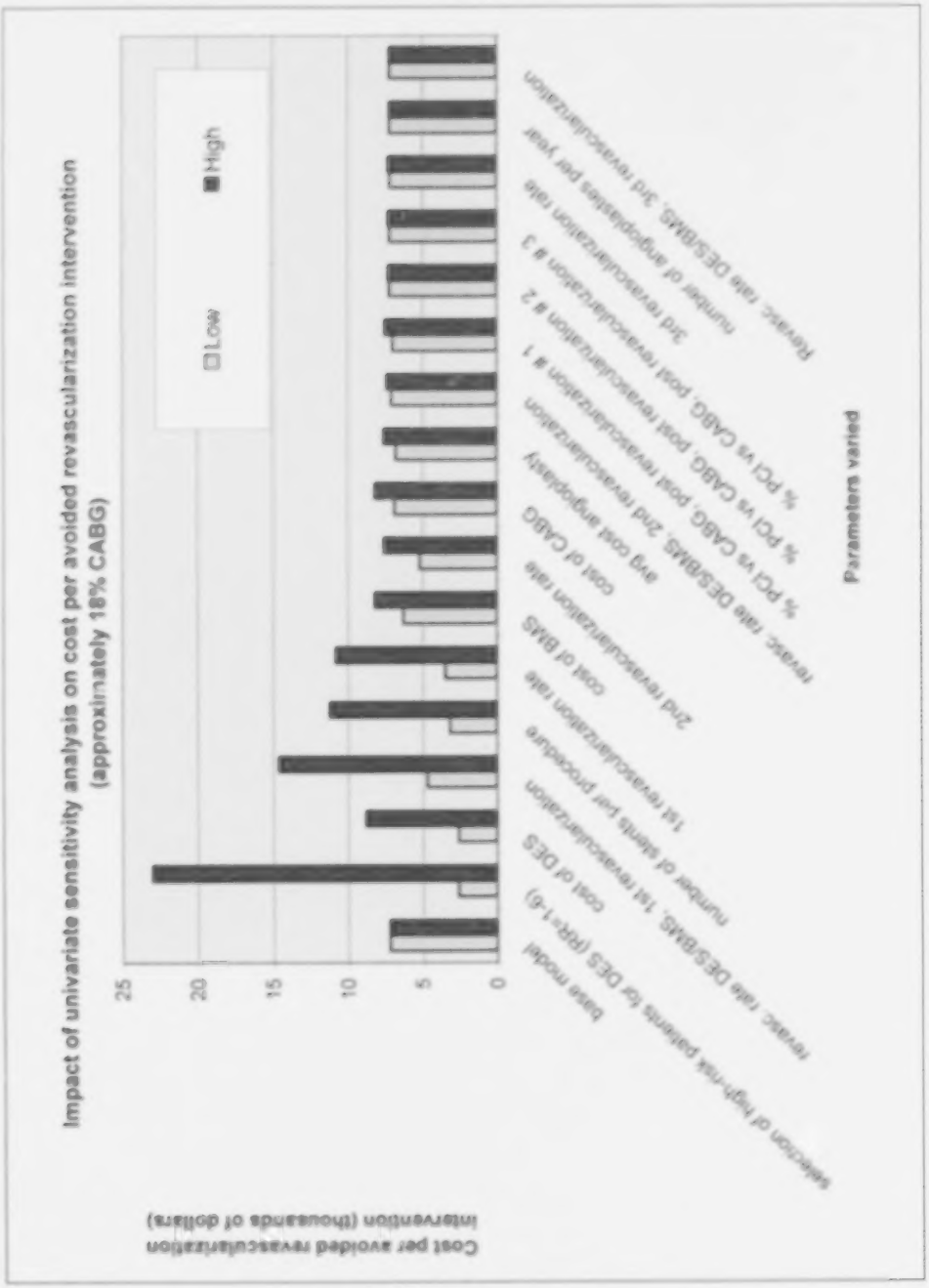
= (534*0.013+534*(0.04+0.02))+(117*0.013+117*0.07)
= (6.942+32.04)+(1.521+8.19)
= 38.982+9.711
= 48.693

Cost per QALY gained= $4.7M / 48.693
= $96 523

# APPENDIX G


Univariate sensitivity analysis, impact on incremental cost
Low
High
Incremental cost (millions of dollars)
8
7
6
5
4
3
2
1
0
base model
cost of DES
selection of high-risk patients
number of stents per procedure
1st revascularization rate
revasc. rate DES/BMS, 1st revascularization
2nd revascularization rate
cost of BMS
# angioplasties/yr
cost of CABG
% PCI vs CABG, post revascularization
average cost of angioplasty
revasc. rate DES/BMS, 3rd revascularization
% PCI vs CABG, 2nd revascularization
revascularization rate DES/BMS, 2nd revascularization
3rd revascularization rate
% PCI vs CABG, post revascularization
revasc. rate DES/BMS, 3rd revascularization
Input paramaters varied

# APPENDIX H


Impact of univariate sensitivity analysis on cost per avoided revascularization intervention
(approximately 18% CABG)
Low
High
25
20
15
10
5
0
Cost per avoided revascularization intervention (thousands of dollars)
Parameters varied
base model
selection of high-risk patients for DES (RR=1.6)
revasc. rate DES/BMS: 1st revascularization
cost of DES
number of stents per procedure
1st revascularization rate
cost of BMS
2nd revascularization rate
cost of CABG
avg cost angioplasty
revasc. rate DES/BMS: 2nd revascularization
% PCI vs CABG: post revascularization # 1
% PCI vs CABG: post revascularization # 2
% PCI vs CABG: post revascularization # 3
3rd revascularization rate
number of angioplasties per year
Revasc. rate DES/BMS: 3rd revascularization

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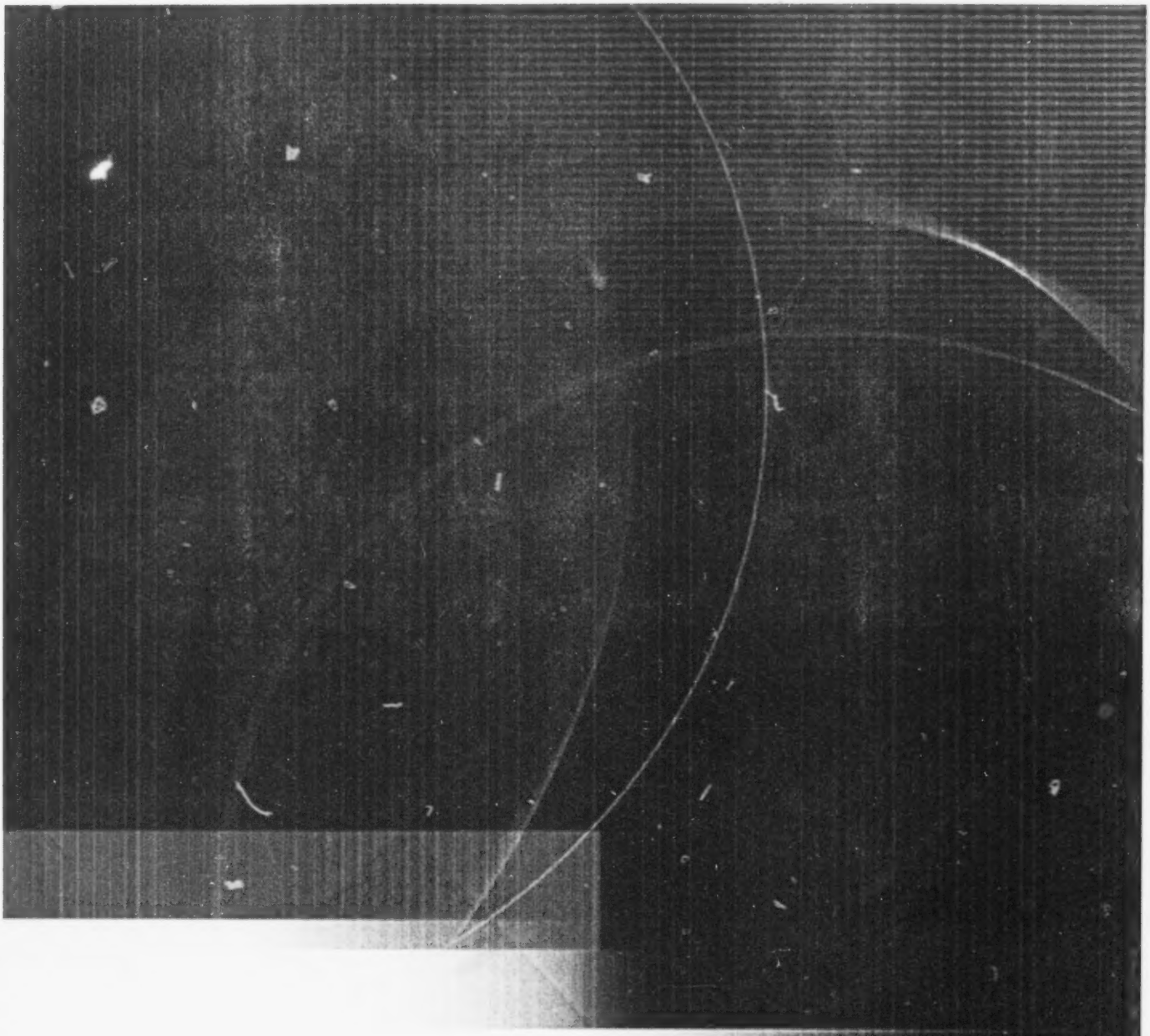

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